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Implementing change control in a regulated pharma environment using discus QMS

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Importance of change control in pharma QMS

Change control is the most crucial element in a pharmaceutical company's quality management system. Inadequate change control procedures create a massive risk of non-compliance for such firms.The importance of change control systems cannot be stressed enough, especially in modern times where rapid upgrades are continually being made in production techniques, engineering, research, and materials being used. The pharma industry's regulatory guidance reinforces the significance of implementing effective change control procedures as a pivotal component of the firm's overall quality system. Moreover, pharmaceutical companies looking to expand globally need to adhere to stringent guidelines laid down by regulatory bodies such as the FDA (for the US) and MHRA (for European Union), which clearly state the need for digitization, data integrity, and compliance in the QMS process.

Pharmaceutical companies looking to expand globally must also adhere to guidelines laid down by the FDA, International Conference of Harmonization (ICH), and other regulatory bodies. They are expected to establish dedicated change control systems that help them improve product quality, safety, and compliance. The Current Good Manufacturing Practice (CGMP) regulations mentioned in the 21 CFR Parts 210-211 also outline that anticipated changes must be evaluated to determine their impact on component quality and validation status.

Pharmaceutical companies often need to make changes to their products or processes to improve their efficiency, quality, or safety measures. Each such modification is reported in the change control process and needs to be approved by QA authorities before being implemented. Without Change Control systems, pharma processes could quickly spiral out of control, leading to major disruptions in productions.

Today, all major players in the pharma industry use quality management systems (QMS) to reduce audit time, standardize product quality, discover deviations, and reduce the probability of product recalls. QMS helps pharma manufacturers observe strict compliance to approved procedures and keep their production operations in control. The Food and Drug Administration (FDA) and several other global regulatory bodies consider QMS critical in the pharmaceutical manufacturing process.

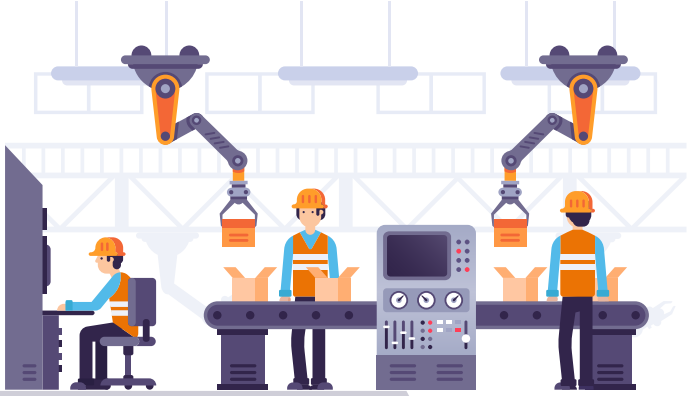
Over the years, most pharmaceutical companies have either used paper-based change management systems (CMS) or a combination of digital and paper-based CMS. The FDA has discouraged using paper-based CMS systems as they can significantly increase the risk of GMP non-compliance. They can also impede a pharmaceutical producer's ability to implement initiatives for continuous improvements in products and processes.

Moreover, paper-based CMS can become a potential bottleneck to rapid growth and capitalization on investments. Thus, modern pharmaceutical companies looking for sustainable expansion with adherence to compliance measures need to switch to paperless CMS.

What is change control?

Change control is an essential component of a pharmaceutical firm's QMS that keeps track of upgrades/updates made in its production, components, quality, and processes.Without them, many pharma producers would encounter a considerable risk of non-compliance, and their overall production quality would be hugely disrupted. Lack of proper change control procedures could not only invite legal consequences, but they could also lead to loss of credibility.

Pharmaceutical companies worldwide need to adhere to strict regulatory standards to ensure their products' quality and safety. Since changes may occur at any given time during a product's life cycle, the impact of (both major and minor) change must be documented, registered, and approved through proper procedures. The impact of each change must also be analyzed (for safety, quality, time, and investment) and balanced against the cost of making each alteration. Moreover, random unapproved changes in components or procedures can cause the final product to fail in the field.



Pharmaceutical companies are required to control any change in their established manufacturing processes - meaning the changes made have to be recorded, assessed for impact, reviewed, and approved by their Quality Assurance (QA) unit. PS 9000: 2001,§,3.7, defines change control as " A process that ensures that changes to material, methods, equipment, and software are properly documented, validated, approved and traceable." The IPAC-RS guideline (§ 3.3) also adds an additional requirement for change control by stating that " The process includes an evaluation to determine whether validation is required and the level of validation required."

Change control is initiated through a documented proposal to record, report, categorize and assess the impact of said changes in existing procedures and systems. The change control proposal assesses how the proposed change may impact safety, quality, purity, identity, the productivity of the drug produced, the facility where the drug is produced, and the overall documentation process.

Advantages of using change control systems

The use of proper change management systems provides the following advantages to pharmaceutical companies:

- Routing of change requests through appropriate authorities/teams for approval
- Digital documentation of approved changes and their implementation

- Tracking of changes and providing an audit trail
- Risk assessment & management
- Better compliance to health authorities and minimal paperwork
- Maintenance of change history, easy information retrieval & detailed documentation of changes that can be shared and accessed instantly
- Standardization of output

Global regulatory requirements for CMS

Effective change management is vital for the successful implementation of quality management systems. In highly regulated environments, strict adherence to approved policies and procedures helps keep manufacturing operations in control and helps standardize production consistency. However, there are specific guidelines that help quality assurance systems become genuinely world-class.

The FDA's 21 CFR guidelines (Part 210-211) make it compulsory for pharmaceutical companies to provide written procedures as part of current good manufacturing practices. Thus, any changes made in production and processes must be recorded, reviewed, and duly authorized by the company's quality control unit.

The Code of Federal Regulations (CFR) mentions two brief notes on the topic of 'change control,' which are:

211.100 Written procedures; deviations

(a) “There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart. These written procedures, including any changes, shall be drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit.”

211.160 General requirements

(a) “The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit. The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.”

Apart from 21CFR, the European Union's Good Manufacturing Process (GMP) also mentions the following guidelines on the topic of change control:

"Significant amendments to the manufacturing process, including any change in equipment or materials, which may affect product quality, as well as the reproducibility of the process, should be validated."

The above guidelines clearly highlight the importance of change control adherence in the pharma industry. Additionally, the Current Good Manufacturing Practice (CGMP) requirements are created to prevent public health damage by mandating quality adherence to medicines' production and development. The ISO 9000:2015 and ISO 13485:2016 certifications also require manufacturers to document and control the alterations made to product design, requirements, and development changes.

Process of change control in the pharmaceutical industry

Before initiating change control, pharmaceutical manufacturers need to clearly define why they want to make the change, provide justification for it, and clearly state the objective for the difference. Quality assurance executives then prepare an SOP (Standard Operating Procedure), and the Assistant Manager of Quality Assurance & Regulatory Affairs has the responsibility of tracking the change control form (CCF).

The department where a change needs to be implemented needs to fill out a (CCF) to initiate the process of change control after which the following steps need to be taken for implementing pharmaceutical change control (see image below):

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Change Identification and Login

Risk/Impact Assessment

Propose Methodology, Supporting documents, Coordinate with other departments and define timelines for Implementation.

Minutes Of Meeting (Change control Assessment)

Minor Change

Action Plan For Implementation (Pre/Post Implementation)

Major / Critical Change

Decision by QA in consultation with Concerned Personnel / Affected Dept.

Change Approved

Notification to HA / QP /MA Holder / Customer

Change Approved

Change Implemented as Proposed / Approved

Change Not Approved

Justification for Disapproval

Change Control Closure

Change History

Responsibilities

To enable change control to take place successfully, there are different sets of responsibilities that have to be shouldered by different departments, which are mentioned below:

1. Initiator's responsibilities:

The change control initiator(s) have the following responsibilities:

- Identification of the change needed, the reason/justification for the change to be done has to be done by the initiating department or individual. After identification, the change request form must be filled with suitable descriptions and reasons for change.
- The impact and risks associated with the change, identification of systems that would be affected and a detailed plan/proposal for risk mitigation must be documented.
- Considering the change and its impact/risk, a methodology for initiating, reviewing and implementation of the changes should be proposed. The initiator must also provide supporting documents and coordinate with all the departments/personnel to be affected.
- An estimated timeline for the proposed change should be provided. Changes which have to be implemented on priority need to be highlighted and justified. If the set timelines can't be adhered, proper justification with prior approval must be provided by the initiating department.

2. QA's responsibilities:

The Quality Assurance team handles the following responsibilities before, after and during the change control process:

- If change control is being managed manually, each change being made must be formally logged. The records must have proper descriptions and be easy to maintain.

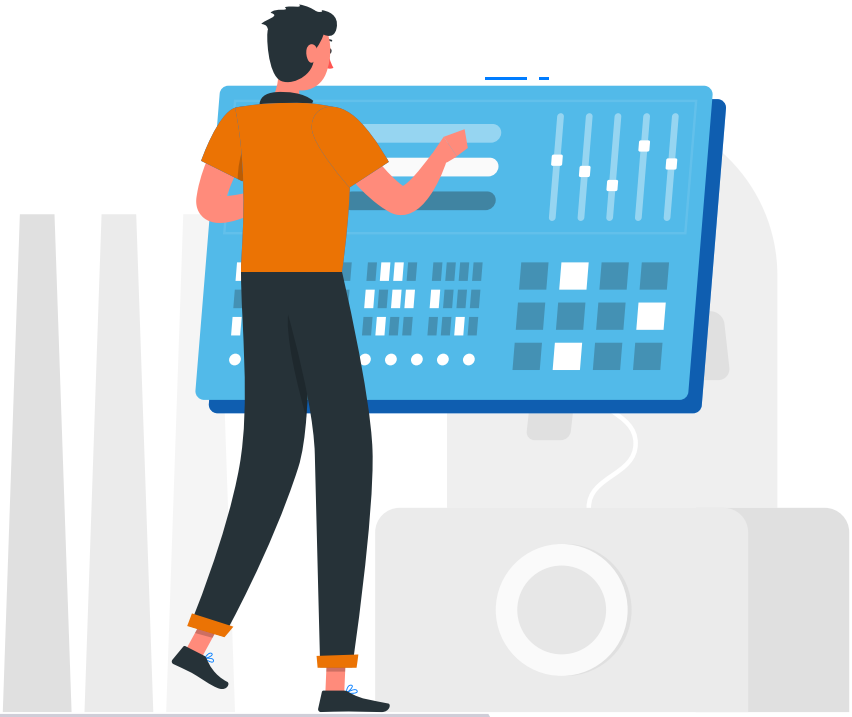
- A proper assessment of the change's impact of product safety, quality, operating procedures, environment, QMS and personnel must be done based on risk analysis. If the change is impacting any one of the above, the change is to be classified as 'critical', 'major' or 'minor'. (The change can be reviewed and approved by individuals in the same function/ department that performed the original review and approval, unless there are specific designations stating otherwise.)

- Based on the degree of risks associated with the change (i.e., critical, major or minor) a detailed plan for implementation is prepared. A detailed account of actions to be taken and their status of completion with respect to the activities involved is tracked.

Scope of change control systems

The scope of a CMS covers a broad set of potential risks, including:

- Changes to product design & formulation
- Standard operating procedure (SOP), analytical test procedures, templates, stability protocols, specifications for biological products
- Planned preventive maintenance of equipment or exchange of components during servicing
- Changes to packaging specifications, labeling, intermediaries shipped as final drug products
- All modifications planned for the alteration, upgradation, deletion, and repair/ replacement of equipment, utility, facility, or area
- Materials, instruments, design, engineering drawings, networks, servers, etc., made or maintained by the pharma manufacturing unit



Implementing change control effectively in a regulated pharma environment

To properly evaluate, approve and implement the changes needed, pharma and clinical supplies companies should have an effective CMS system that ensures continuous improvements undertaken in a timely, prioritized, and effective way. The CMS must offer a high degree of assurance that there are no unintended consequences of the changes made.

For effective implementation of CMS, it must include the following:

- Quality risk management should be utilized to evaluate the proposed changes, and the level of effort and formality of evaluation must be commensurate with the level of risk involved. There should also be an assessment to determine if a change to the regulatory filing is needed under regional requirements.

- All proposed changes must be evaluated relative to the marketing authorization, including the design space where the change was established and/or the current process and product understanding. While the ICH Q8 mentions that movements within the design space are not considered to be a change from a regulatory filing standpoint, from a pharmaceutical QMS perspective, all changes need to be evaluated by a firm's CMS.

- The proposed changes should be evaluated carefully by expert teams with proper knowledge in relevant areas such as manufacturing, pharmaceutical development, quality, medicine, and regulatory affairs to ensure that the change is technically justified. The prospective evaluation criteria for proposed changes should also be set.

- After implementation, an assessment of the impact of the change should be undertaken to confirm that the change objectives were achieved and no negative impact was observed on the product's quality.

- Regional regulatory approval/submission requirements should be assessed for a proposed change to marketed products.

- The CMS should also ensure that the level of effort and documentation matches the level of risks associated with the change. Pharmaceutical companies should ensure that the CMS:

  01 Is linked and fully integrated with other QMS systems such as CAPA, validation, consumer complaints, etc.

  02 Includes evaluation criteria to determine if changes are technically justified

  03 Includes criteria to verify whether changes affect a regulatory filing

  04 Houses procedures for validating and confirming that the change has successfully taken place, the objectives were achieved, and there were no unintended consequences

  05 Include criteria to check effectiveness of change control

  06 Develops a change control tracking system to facilitate effective change management.

For proper implementation of CMS, significant cultural and organizational barriers must also be addressed. QMS teams in life science companies need to be more agile, organized and offer an enterprise-wide response to changes made. Teams should meet often and use an appropriate set of metrics that track changes and drive process improvements smoothly.

Choosing the right QMS partner for your firm

Giant strides are being taken in the field of medicine each day. Firms require a reliable QMS solution that offers the following features:

Highly-configurable:

The QMS solution should be highly configurable to suit your organization's unique needs and demands.

Data Integrity & Compliance:

The QMS software should be validated and compliant with 21 CFR Part 11 guidelines. All activities in the QMS should be traceable and have detailed audit trails.

Documented Justifications:

The solution requires proper justification for changes that are made. The reasons for making the change should also be documented.

Automation, Notification & Escalations:

The solution should route documents automatically, seek necessary approvals/e-signatures, have notification and escalation procedures, and be able to search and retrieve documents easily.

Centralized Repository:

The QMS solution must centralize and digitize information so that authorities can find the information they need easily. It should be able to handle multiple file types required in the QMS process.

Continuous Improvement:

The system/software should also enable timely compliance reviews (of logbooks reviewed, complaints managed, CR- cases closed, internal audit reports closed, etc.) to be done by a notification report.

How discus QMS can help in change control implementation

Discus Business Solutions (DBS) brings a combination of technical expertise, hands-on experience, and industry knowledge needed to implement its software solutions successfully in the pharmaceutical industry. With over a decade of experience in providing customized software solutions to leading multinational pharmaceutical clients. With its extensive expertise in QMS, it assists pharmaceutical firms in proper documentation and management of change control processes with configurable permissions based on user roles.

Discus QMS has been carefully designed, keeping the above requirements in mind. Along with a 21 CFR Part 11) certification for compliance, it also offers a highly configurable and user-friendly interface besides adhering to several industry best-practices.

It also offers features like email integration, audit history, configurable workflows, email integration, and real-time event tracking. This aids in streamlining change control effectively and adhering to set guidelines.

Discus Pharma QMS has real-time notifications, customizable reports, and audit trails. It is a business asset that ensures you never miss any update and progress on the path of continuous growth and advancement.

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